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(FILE 'HOME' ENTERED AT 17:46:19 ON 15 FEB 2006)

FILE 'HCAPLUS' ENTERED AT 17:46:32 ON 15 FEB 2006

E CHOW KEN/AU
L1 27 SEA ABB=ON "CHOW KEN"/AU
E GIL DANIEL W/AU
L2 50 SEA ABB=ON ("GIL DANIEL"/AU OR "GIL DANIEL W"/AU OR "GIL
DANIEL WALTER"/AU)
E FANG WENKUI KEN/AU
L3 7 SEA ABB=ON ("FANG WENKUI"/AU OR "FANG WENKUI KEN"/AU)
E GARST MICHAEL/AU
L4 114 SEA ABB=ON ("GARST MICHAEL"/AU OR "GARST MICHAEL E"/AU OR
"GARST MICHAEL ELWOOD"/AU)
E WHEELER LARRY A/AU
L5 64 SEA ABB=ON ("WHEELER LARRY A"/AU OR "WHEELER LARRY ALLEN"/AU)
L6 4 SEA ABB=ON L1 AND L2 AND L3 AND L4 AND L5
SELECT RN L6 1-4
SELECT RN L6 1

FILE 'REGISTRY' ENTERED AT 17:48:24 ON 15 FEB 2006

L7 5 SEA ABB=ON (366786-91-6/BI OR 141-43-5/BI OR 2740-88-7/BI OR
366787-56-6/BI OR 61290-32-2/BI)

FILE 'HCAPLUS' ENTERED AT 17:48:30 ON 15 FEB 2006

L8 4 SEA ABB=ON L6 AND L7

FILE 'REGISTRY' ENTERED AT 17:49:31 ON 15 FEB 2006

L9 STRUCTURE 366786-91-6 — *located via Inventor Search*
L10 1 SEA SSS SAM L9
L11 7 SEA SSS FUL L9 *7 compds from Reg. See attached "I guess that" for structure*

FILE 'HCAPLUS' ENTERED AT 17:50:12 ON 15 FEB 2006

L12 7 SEA ABB=ON L11
L13 4 SEA ABB=ON L12 AND (PRD<20011019 OR PD<20011019) *4 cit's from CA Plus*

FILE 'USPATFULL' ENTERED AT 17:56:18 ON 15 FEB 2006

L14 0 SEA ABB=ON L12 AND (PRD<20011019 OR PD<20011019) *0 cit's in USPatfull*

FILE HOME

FILE HCAPLUS

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FILE COVERS 1907 - 15 Feb 2006 VOL 144 ISS 8
FILE LAST UPDATED: 14 Feb 2006 (20060214/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 FEB 2006 HIGHEST RN 874270-88-9

DICTIONARY FILE UPDATES: 14 FEB 2006 HIGHEST RN 874270-88-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
*
*****
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 14 Feb 2006 (20060214/PD)

FILE LAST UPDATED: 14 Feb 2006 (20060214/ED)

HIGHEST GRANTED PATENT NUMBER: US7000250

HIGHEST APPLICATION PUBLICATION NUMBER: US2006031974

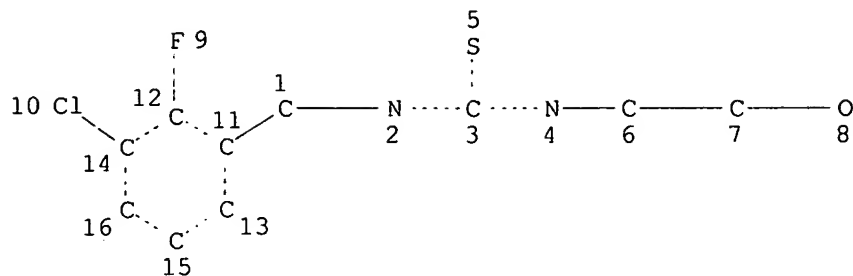
CA INDEXING IS CURRENT THROUGH 14 Feb 2006 (20060214/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 14 Feb 2006 (20060214/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

=> d que stat l13
L9 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L11 7 SEA FILE=REGISTRY SSS FUL L9
L12 7 SEA FILE=HCAPLUS ABB=ON L11
L13 4 SEA FILE=HCAPLUS ABB=ON L12 AND (PRD<20011019 OR PD<20011019)

=> d ibib abs hitstr l13 1-4

L13 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:521523 HCAPLUS

DOCUMENT NUMBER: 137:73273

TITLE: Adrenergic receptor ligand-neurotoxin conjugates and methods for treating pain

INVENTOR(S): Gil, Daniel W.; Aoki, Kei Roger

PATENT ASSIGNEE(S): Allergan Sales, Inc., USA

SOURCE: PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053177	A2	20020711	WO 2001-US48651	20011214 <--
WO 2002053177	A3	20030918		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 6787517	B1	20040907	US 2000-751053	20001229
CA 2433332	AA	20020711	CA 2001-2433332	20011214 <--
EP 1363674	A2	20031126	EP 2001-990212	20011214 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2005506277	T2	20050303	JP 2002-554126	20011214 <--
US 2004146532	A1	20040729	US 2004-791434	20040301 <--
PRIORITY APPLN. INFO.:			US 2000-751053	A 20001229 <--
			WO 2001-US48651	W 20011214

OTHER SOURCE(S): MARPAT 137:73273

AB Agents for treating pain, methods for producing the agents, and methods for treating pain by administration to a patient of a therapeutically effective amount of the agent, are disclosed. The agent may include a clostridial neurotoxin, a fragment or a derivative thereof, attached to a targeting component, wherein the targeting component is selected from a group consisting of compds. which selectively binds at the $\alpha 2b$ or $\alpha 2b/\alpha 2c$ adrenergic receptor subtype(s) as compared to other binding sites, e.g. the $\alpha 2a$ adrenergic receptor subtype.

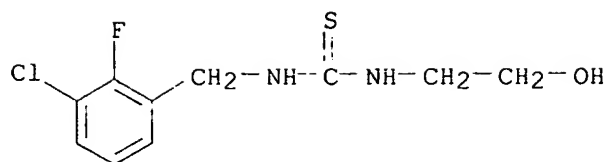
IT 366786-91-6D, conjugates

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adrenergic receptor ligand-neurotoxin conjugates and methods for treating pain)

RN 366786-91-6 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:369027 HCAPLUS

DOCUMENT NUMBER: 136:363872

TITLE: Preparation of thiourea compounds for modulating α -adrenergic receptor activity and use in the treatment of pain

INVENTOR(S): Chow, Ken; Gil, Daniel W.; Fang, Wenkui; Garst, Michael E.; Wheeler, Larry A.

PATENT ASSIGNEE(S): Allergan Sales, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 548,315, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent

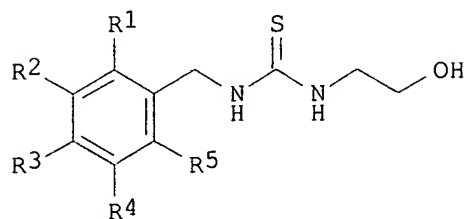
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002058839	A1	20020516	US 2001-778975	20010205 <--
US 6545182	B2	20030408		
PRIORITY APPLN. INFO.:			US 2000-548315	B2 20000413 <--
OTHER SOURCE(S):	MARPAT	136:363872		

GI



I

AB Methods and compns. are disclosed which use thiourea compds. I (R1, R5 = halo, alkyl, alkoxy, etc.; R2, R4 = halo, alkyl, alkoxy, etc.; R3 = F, H), and alkyl esters thereof, for the treatment of pain. Preparation of I [R1 = F; R2 = Cl; R3-R5 = H] which showed EC50 of 16 nM and 457 nM at α 2B and α 2C receptor in RSAT assay, was given. Particularly disclosed are compns. for the treatment of chronic pain, and methods for their use.

IT 366786-91-6P 366786-99-4P 366787-14-6P

366787-16-8P 366787-23-7P 366787-38-4P

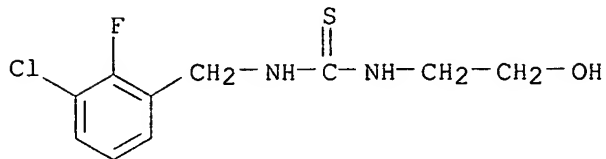
366787-39-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of thiourea compds. for modulating α -adrenergic receptor

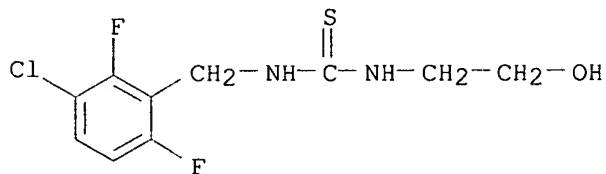
activity and use in treatment of pain)

RN 366786-91-6 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI)
(CA INDEX NAME)

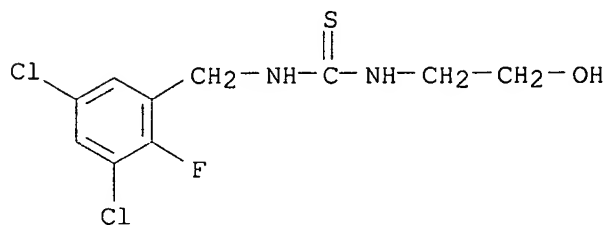
RN 366786-99-4 HCAPLUS

CN Thiourea, N-[(3-chloro-2,6-difluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



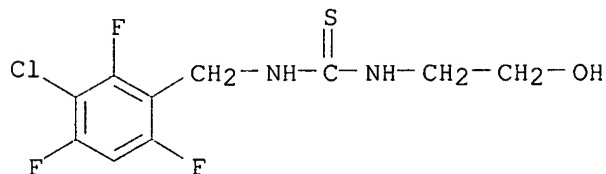
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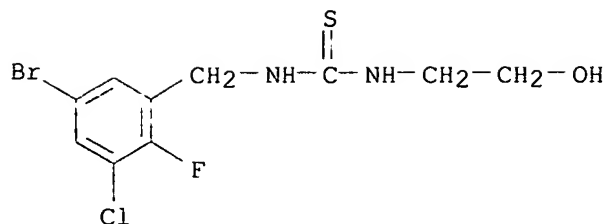
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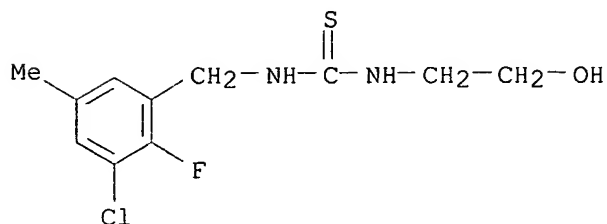


RN 366787-23-7 HCAPLUS

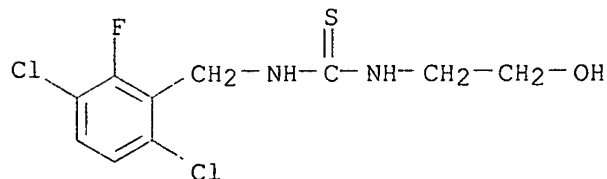
CN Thiourea, N-[(5-bromo-3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 366787-38-4 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluoro-5-methylphenyl)methyl]-N'-(2-hydroxyethyl)-
(9CI) (CA INDEX NAME)

RN 366787-39-5 HCAPLUS

CN Thiourea, N-[(3,6-dichloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)-
(9CI) (CA INDEX NAME)

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:780662 HCAPLUS

DOCUMENT NUMBER: 135:327361

TITLE: Methods and compositions using benzylthiourea
derivatives for modulating alpha adrenergic receptor
activityINVENTOR(S): Chow, Ken; Gil, Daniel W.; Fang, Wenkui Ken; Garst,
Michael E.; Wheeler, Larry A.

PATENT ASSIGNEE(S): Allergan Sales, Inc., USA

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078703	A2	20011025	WO 2001-US11843	20010411 <--
WO 2001078703	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6313172	B1	20011106	US 2000-548410	20000413
CA 2406057	AA	20011025	CA 2001-2406057	20010411 <--
EP 1280525	A2	20030205	EP 2001-926876	20010411 <--
EP 1280525	B1	20050209		

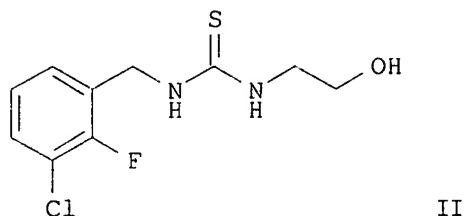
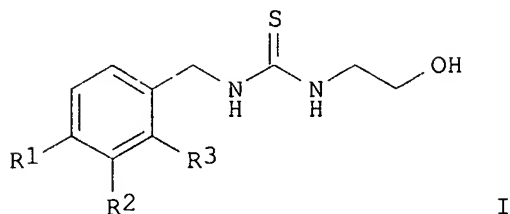
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JP 2003530430	T2	20031014	JP 2001-576004	20010411 <--
NZ 522027	A	20041126	NZ 2001-522027	20010411 <--
AT 288747	E	20050215	AT 2001-926876	20010411 <--
ES 2233627	T3	20050616	ES 2001-1926876	20010411 <--
HK 1051324	A1	20050916	HK 2003-103605	20030521 <--

PRIORITY APPLN. INFO.:

US 2000-548410	A	20000413 <--
WO 2001-US11843	W	20010411 <--

OTHER SOURCE(S): MARPAT 135:327361
GI

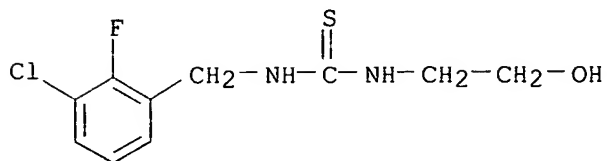


AB The invention discloses benzylthiourea derivs. I (R1, R3 = F, H; R2 = Cl, H; with provisos, and alkyl esters thereof) as α 2-adrenergic receptor modulators. The invention also describes the synthesis of a compound II (wherein R1= H, R2= Cl and R3 = F). The effects of these disclosed compds. on acute and chronic pain, their sedative action and their cardiovascular effects are described.

IT **366786-91-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzylthiourea derivs. for modulating alpha adrenoceptor activity and their application in pain therapy)

RN 366786-91-6 HCAPLUS
 CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI)
 (CA INDEX NAME)



RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(benzylthiourea derivs. for modulating alpha adrenoceptor activity and their application in pain therapy)

L13 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:780661 HCAPLUS

DOCUMENT NUMBER: 135:298811

TITLE: Thiourea compounds for modulating α -adrenergic receptor activity, preparation, compositions, and use in the treatment of pain

INVENTOR(S): Chow, Ken; Gil, Daniel W.; Fang, Wenkui Ken; Garst, Michael E.; Wheeler, Larry A.

PATENT ASSIGNEE(S): Allergan Sales, Inc., USA

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

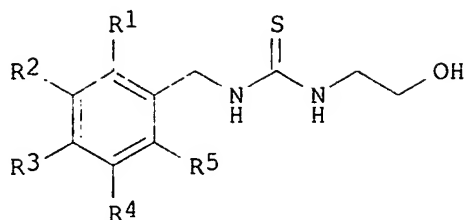
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078702	A2	20011025	WO 2001-US11842	20010411 <--
WO 2001078702	A3	20020321		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2405796	AA	20011025	CA 2001-2405796	20010411 <--
EP 1280524	A2	20030205	EP 2001-926875	20010411 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003530429	T2	20031014	JP 2001-576003	20010411 <--
PRIORITY APPLN. INFO.:			US 2000-548315	A 20000413 <--
			WO 2001-US11842	W 20010411 <--
OTHER SOURCE(S):	MARPAT 135:298811			
GI				



I

AB Methods and compns. are disclosed which use thiourea compds. I (R1, R2, R4, R5 = H, OH, Cl-3 alkyl, etc.; R3 = H, F), and alkyl esters thereof, for the treatment of pain. Particularly disclosed are compns. for the treatment of chronic pain, and methods for their use.

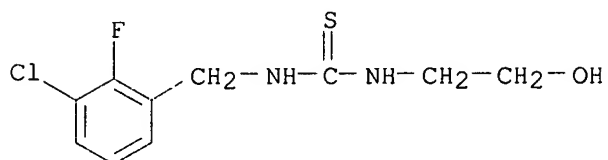
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366787-16-8 366787-23-7 366787-38-4
366787-39-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiourea compds. for modulating α -adrenergic receptor activity, preparation, compns., and use in treatment of pain)

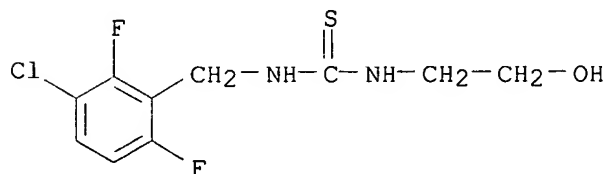
RN 366786-91-6 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI)
(CA INDEX NAME)



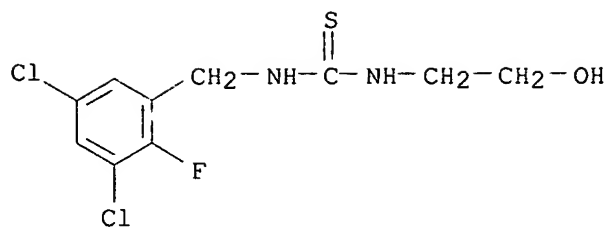
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CN Thiourea, N-[(3-chloro-2,6-difluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



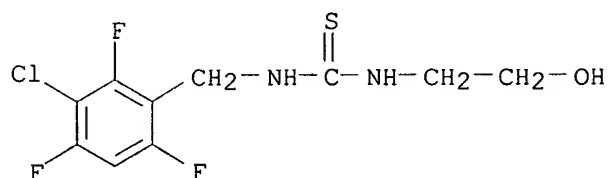
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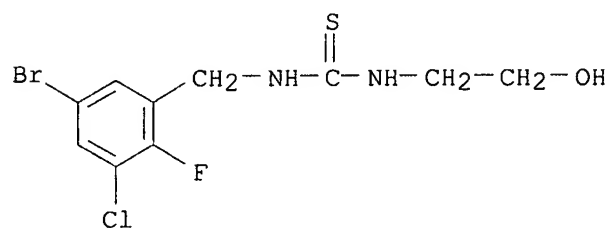
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(9CI) (CA INDEX NAME)



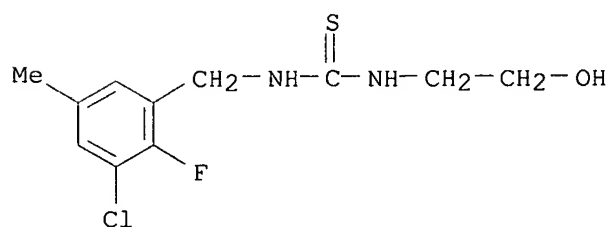
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(9CI) (CA INDEX NAME)



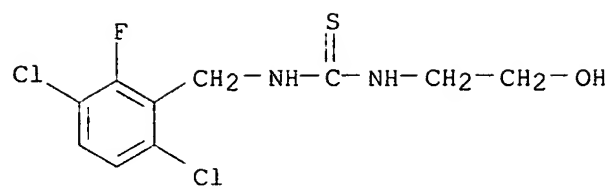
RN 366787-38-4 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluoro-5-methylphenyl)methyl]-N'-(2-hydroxyethyl)-
(9CI) (CA INDEX NAME)



RN 366787-39-5 HCAPLUS

CN Thiourea, N-[(3,6-dichloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)-
(9CI) (CA INDEX NAME)



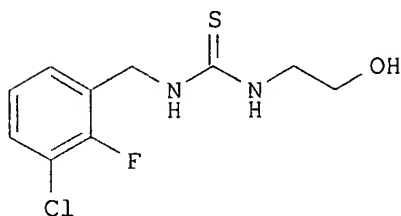
Fay 10/039,827

15/02/2006

=> d ibib abs hitstr l8 1-4

L8 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:334962 HCAPLUS
DOCUMENT NUMBER: 138:331737
TITLE: Methods and compositions for modulating α
adrenergic receptor activity, and therapeutic use
thereof
INVENTOR(S): Chow, Ken; Gil, Daniel W.;
Fang, Wenkui Ken; Garst, Michael E.;
Wheeler, Larry A.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035178	A1	20030501	WO 2002-US32571	20021011
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003092766	A1	20030515	US 2001-39827	20011019
PRIORITY APPLN. INFO.:			US 2001-39827	A 20011019
OTHER SOURCE(S):	MARPAT 138:331737			
GI				



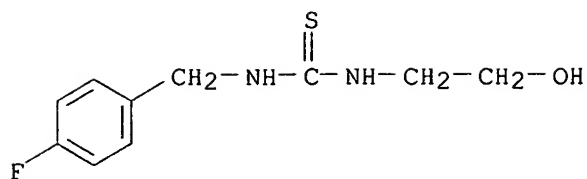
AB Methods and compns. are discloses for the treatment of pain and intraocular pressure. Particularly disclosed are compns. for the treatment of chronic pain, glaucoma, and methods for their use. Compds. of the invention include e.g. I (preparation given).

IT **61290-32-2P 366786-91-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiourea derivs., preparation and use in treatment of glaucoma and pain)

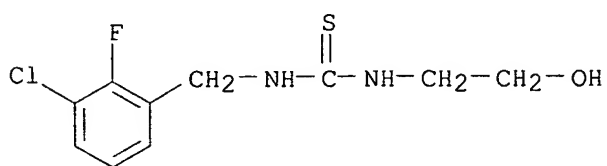
RN 61290-32-2 HCAPLUS

CN Thiourea, N-[(4-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX

NAME)



RN 366786-91-6 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI)
(CA INDEX NAME)RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(thiourea derivs., prepn. and use in treatment of glaucoma and pain)

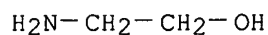
IT 141-43-5, Ethanolamine, reactions 2740-88-7,
4-Fluorobenzyl isothiocyanate 366787-56-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(thiourea derivs., preparation and use in treatment of glaucoma and pain)

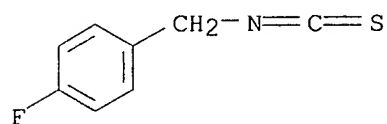
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CN Ethanol, 2-amino- (8CI, 9CI) (CA INDEX NAME)

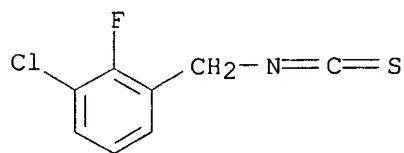


RN 2740-88-7 HCAPLUS

CN Benzene, 1-fluoro-4-(isothiocyanatomethyl)- (9CI) (CA INDEX NAME)



RN 366787-56-6 HCAPLUS

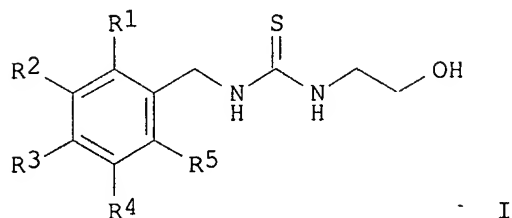
CN Benzene, 1-chloro-2-fluoro-3-(isothiocyanatomethyl)- (9CI) (CA INDEX
NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:369027 HCAPLUS
 DOCUMENT NUMBER: 136:363872
 TITLE: Preparation of thiourea compounds for modulating α -adrenergic receptor activity and use in the treatment of pain
 INVENTOR(S): Chow, Ken; Gil, Daniel W.; Fang, Wenkui; Garst, Michael E.; Wheeler, Larry A.
 PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 548,315, abandoned.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002058839	A1	20020516	US 2001-778975	20010205
US 6545182	B2	20030408		
PRIORITY APPLN. INFO.:			US 2000-548315	B2 20000413
OTHER SOURCE(S):	MARPAT	136:363872		

GI

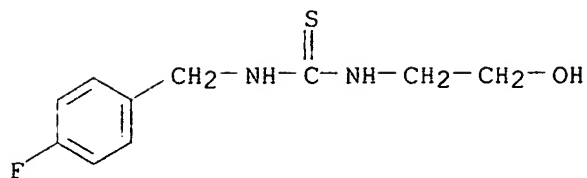


AB Methods and compns. are disclosed which use thiourea compds. I (R1, R5 = halo, alkyl, alkoxy, etc.; R2, R4 = halo, alkyl, alkoxy, etc.; R3 = F, H), and alkyl esters thereof, for the treatment of pain. Preparation of I [R1 = F; R2 = Cl; R3-R5 = H] which showed EC50 of 16 nM and 457 nM at α 2B and α 2C receptor in RSAT assay, was given. Particularly disclosed are compns. for the treatment of chronic pain, and methods for their use.

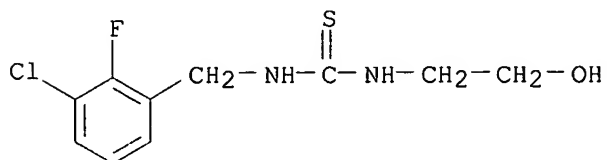
IT **61290-32-2P 366786-91-6P**
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of thiourea compds. for modulating α -adrenergic receptor activity and use in treatment of pain)

RN 61290-32-2 HCAPLUS

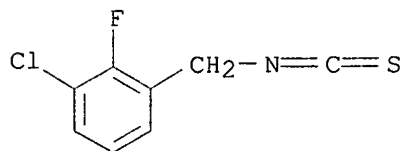
CN Thiourea, N-[(4-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 366786-91-6 HCAPLUS
 CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI)
 (CA INDEX NAME)



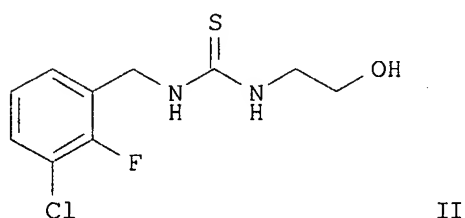
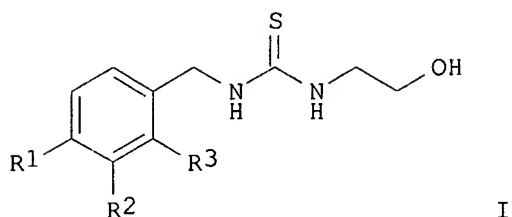
IT 366787-56-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; preparation of thiourea compds. for modulating α -adrenergic
 receptor activity and use in treatment of pain)
 RN 366787-56-6 HCAPLUS
 CN Benzene, 1-chloro-2-fluoro-3-(isothiocyanatomethyl)- (9CI) (CA INDEX
 NAME)



L8 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:780662 HCAPLUS
 DOCUMENT NUMBER: 135:327361
 TITLE: Methods and compositions using benzylthiourea
 derivatives for modulating alpha adrenergic receptor
 activity
 INVENTOR(S): Chow, Ken; Gil, Daniel W.;
 Fang, Wenkui Ken; Garst, Michael E.;
 Wheeler, Larry A.
 PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
 SOURCE: PCT Int. Appl., 28 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078703	A2	20011025	WO 2001-US11843	20010411

WO 2001078703 A3 20020321
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 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 US 6313172 B1 20011106 US 2000-548410 20000413
 CA 2406057 AA 20011025 CA 2001-2406057 20010411
 EP 1280525 A2 20030205 EP 2001-926876 20010411
 EP 1280525 B1 20050209
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2003530430 T2 20031014 JP 2001-576004 20010411
 NZ 522027 A 20041126 NZ 2001-522027 20010411
 AT 288747 E 20050215 AT 2001-926876 20010411
 ES 2233627 T3 20050616 ES 2001-1926876 20010411
 HK 1051324 A1 20050916 HK 2003-103605 20030521
 PRIORITY APPLN. INFO.: US 2000-548410 A 20000413
 OTHER SOURCE(S): MARPAT 135:327361 WO 2001-US11843 W 20010411
 GI



AB The invention discloses benzylthiourea derivs. I (R1, R3 = F, H; R2 = Cl, H; with provisos, and alkyl esters thereof) as α 2-adrenergic receptor modulators. The invention also describes the synthesis of a compound II (wherein R1= H, R2= Cl and R3 = F). The effects of these disclosed compds. on acute and chronic pain, their sedative action and their cardiovascular effects are described.

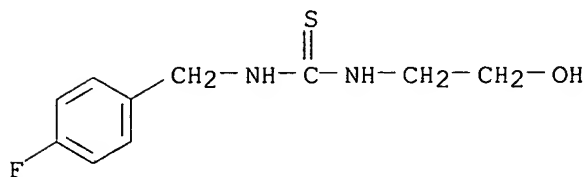
IT 61290-32-2P 366786-91-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (benzylthiourea derivs. for modulating alpha adrenoceptor activity and

their application in pain therapy)

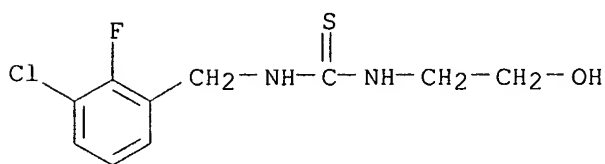
RN 61290-32-2 HCAPLUS

CN Thiourea, N-[(4-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 366786-91-6 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



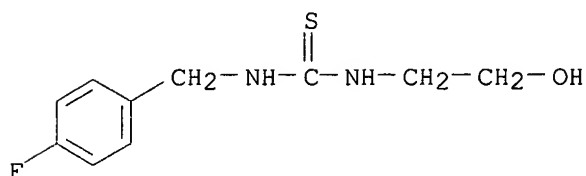
IT 61290-32-2D, alkyl esters 366786-91-6D, alkyl esters

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(benzylthiourea derivs. for modulating alpha adrenoceptor activity and their application in pain therapy)

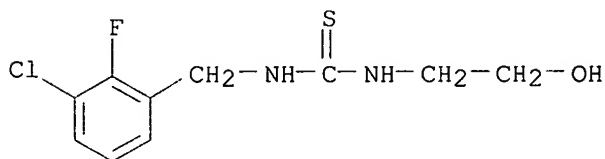
RN 61290-32-2 HCAPLUS

CN Thiourea, N-[(4-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 366786-91-6 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



IT 141-43-5, Ethanolamine, reactions 2740-88-7, 4-Fluoro

benzyl isothiocyanate 366787-56-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(benzylthiourea derivs. for modulating alpha adrenoceptor activity and their application in pain therapy)

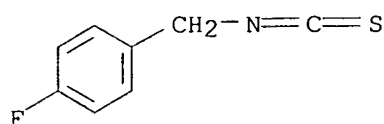
RN 141-43-5 HCAPLUS

CN Ethanol, 2-amino- (8CI, 9CI) (CA INDEX NAME)

 $\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{OH}$

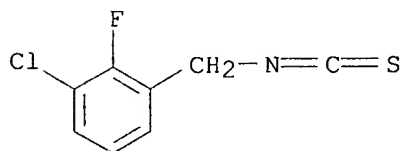
RN 2740-88-7 HCAPLUS

CN Benzene, 1-fluoro-4-(isothiocyanatomethyl)- (9CI) (CA INDEX NAME)



RN 366787-56-6 HCAPLUS

CN Benzene, 1-chloro-2-fluoro-3-(isothiocyanatomethyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:780661 HCAPLUS

DOCUMENT NUMBER: 135:298811

TITLE: Thiourea compounds for modulating α -adrenergic receptor activity, preparation, compositions, and use in the treatment of painINVENTOR(S): Chow, Ken; Gil, Daniel W.;
Fang, Wenkui Ken; Garst, Michael E.;
Wheeler, Larry A.

PATENT ASSIGNEE(S): Allergan Sales, Inc., USA

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

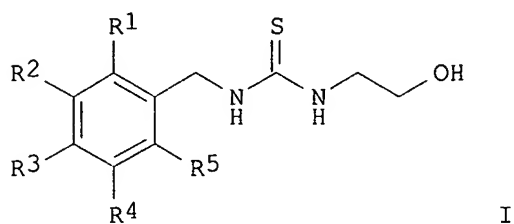
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078702	A2	20011025	WO 2001-US11842	20010411
WO 2001078702	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

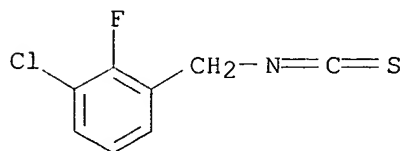
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
 ZA, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2405796 AA 20011025 CA 2001-2405796 20010411
 EP 1280524 A2 20030205 EP 2001-926875 20010411
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2003530429 T2 20031014 JP 2001-576003 20010411
 PRIORITY APPLN. INFO.: US 2000-548315 A 20000413
 WO 2001-US11842 W 20010411
 OTHER SOURCE(S): MARPAT 135:298811
 GI



AB Methods and compns. are disclosed which use thiourea compds. I (R1, R2, R4, R5 = H, OH, C1-3 alkyl, etc.; R3 = H, F), and alkyl esters thereof, for the treatment of pain. Particularly disclosed are compns. for the treatment of chronic pain, and methods for their use.
 IT **141-43-5**, Ethanolamine, reactions **366787-56-6**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; thiourea compds. for modulating α -adrenergic receptor activity, preparation, compns., and use in treatment of pain)
 RN 141-43-5 HCAPLUS
 CN Ethanol, 2-amino- (8CI, 9CI) (CA INDEX NAME)

$\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{OH}$

RN 366787-56-6 HCAPLUS
 CN Benzene, 1-chloro-2-fluoro-3-(isothiocyanatomethyl)- (9CI) (CA INDEX NAME)

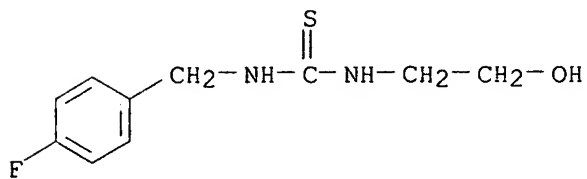


IT **61290-32-2 366786-91-6**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (thiourea compds. for modulating α -adrenergic receptor activity,

preparation, compns., and use in treatment of pain)

RN 61290-32-2 HCAPLUS

CN Thiourea, N-[(4-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 366786-91-6 HCAPLUS

CN Thiourea, N-[(3-chloro-2-fluorophenyl)methyl]-N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

